

Claims 27-37 have been canceled. New claims 38-64 are fully supported by the specification, for example, at page 20, which lists the recited enzymes, the introns and genes encoding them, and references, and in Fig. 6, which shows the recognition sites for each of the recited enzymes. No new matter enters by amendment. Upon amendment, claims 38-64 are pending in this application.

Claim 27 was rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. The Office contends that the recitations of "having at least one HO endonuclease or Group I intron encoded endonuclease site inserted at a unique location in a chromosome" and "said endonuclease" are unclear. The Office also contends that claim 27 is indefinite in that it lacks antecedent basis for "the chromosomal DNA."

Applicants traverse the rejection. Applicants submit that the skilled artisan would recognize that claim 27 refers to an HO endonuclease site. In addition, antecedent basis for "the chromosomal DNA" can be found in the chromosome of step (a). Nonetheless, new claim 38 recites an "at least one HO endonuclease recognition site." Also, new claims 38 and 44 do not recite "the chromosomal DNA." Accordingly, withdrawal of the rejection is respectfully requested.

Claims 33 and 34 were rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite in the recitations of "said endonuclease site" and "said endonuclease recognition site."

Applicants traverse the rejection. Applicants submit that the skilled artisan would recognize that claims 33 and 34 refer to the endonuclease *recognition* site. Nonetheless, new claims 38-64 use the phrase "said endonuclease recognition site." Accordingly, withdrawal of the rejection is respectfully requested.

Claims 27-37 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter that was not described in the specification in such a way as to enable the skilled artisan to make and/or use the invention. The Office contends that the specification does not teach how to use HO endonuclease or Group I intron encoded endonucleases to perform the genetic recombination of the instant claims. The Office alleges that the specification does not characterize what these groups of enzymes are, what their characteristics are, or which enzymes are member of these groups. The Office contends that Figure 6 does not point out which endonucleases are Group I intron encoded endonucleases and which are related endonucleases. The Office concludes that "[t]he specification does not teach that any or all members of these two groups of enzymes can be used for the method of the instant claims, absent convincing proof to the contrary." (Paper No. 5 at 4.)

Applicants traverse the rejection.

The Office has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1561, 27 U.S.P.Q. 2d 1510, 1515 (Fed. Cir. 1993). In addition, M.P.E.P. § 2164.02 states:

For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled

in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation. **Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation.**

Furthermore, M.P.E.P. § 2164.04 states:

While the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection. The language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims. **This can be done by making specific findings of fact, supported by the evidence, and then drawing conclusions based on these findings of fact.** For example, doubt may arise about enablement because information is missing about one or more essential parts or relationships between parts which one skilled in the art could not develop without undue experimentation. In such a case, the examiner should specifically identify what information is missing and why one skilled in the art could not supply the information without undue experimentation. See MPEP 2164.06(a). **References should be supplied if possible to support a prima facie case of lack of enablement, but are not always required.** In re Marzocchi , 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). **However, specific technical reasons are always required.**

Applicants submit that the Office has not met its burden since the Office has not explained **why** one skilled in the art could not make and use the claimed invention without undue experimentation. In contravention of M.P.E.P. § 2164.02, no reasons have been advanced by the Office to establish that a person skilled in the art could not use the genus as a whole without undue experimentation. In contravention of M.P.E.P. § 2164.04, no specific technical reasons have been provided by the Office to

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

support its position. Rather, the Office appears to support the rejection merely concluding that applicants have not taught how to use the claimed invention and then placing the burden on applicants to provide convincing proof to the contrary. Applicants submit that this is insufficient to support the rejection and request withdrawal of the rejection.

No

Moreover, applicants provide detailed teachings regarding the claimed methods. Applicants provide I-SceI as an example of a Group I intron encoded endonuclease for use in the claimed method. Applicants teach that I-SceI is one of a number of enzymes with similar properties. (Specification at 20, lines 5-7.) Applicants provide a list of Group I intron encoded endonucleases and related enzymes on page 20. These include Group I intron encoded endonucleases I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-Csml, I-PanI, I-TevI, I-TevII, and I-TevIII endonucleases. (*Id.* at 20.) Applicants teach the introns encoding these enzymes. (*Id.*) Applicants also teach that HO and Endo SceI are encoded by yeast genes. (*Id.*) Fig. 6 indicates that that HO and Endo SceI are "non-intronic." The "intron site" for each of I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-Csml, I-PanI, I-TevI, I-TevII, and I-TevIII endonucleases is indicated in Fig. 6. The title of Fig. 6 indicates that this figure shows Group I intron encoded endonucleases and related endonucleases. The skilled artisan would understand that I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-Csml, I-PanI, I-TevI, I-TevII, and I-TevIII endonucleases are Group I intron encoded endonucleases and HO and Endo SceI are related endonucleases.

C

Furthermore, applicants teach that the Group I intron encoded endonucleases can be classified on the basis of certain characteristics into Classes I-V. (*Id.* at 21.) Applicants teach that I-SceI, I-SceII, I-SceIII, I-SceIV, I-CsmI, I-CeuI, I-PanI, and I-CreI are Class I Group I intron encoded endonucleases. (*Id.*) Applicants teach that I-TevI is a Class II Group I intron encoded endonuclease. (*Id.*) Applicants teach that I-PpoI is a Class III Group I intron encoded endonuclease. (*Id.*) Applicants teach that I-TevII is a Class IV Group I intron encoded endonuclease. (*Id.*) Applicants teach that I-TevIII is a Class V Group I intron encoded endonuclease. (*Id.*)

In Fig. 6, applicants teach the nucleotide sequences of recognition sites for numerous Group I intron encoded endonucleases including I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-TevII, and I-TevIII endonucleases.

There can be no doubt that the specification discloses numerous Group I intron encoded endonuclease sites. Accordingly, applicants submit that the claimed invention is fully enabled and respectfully request withdrawal of the rejection.

Applicants submit that the application is in condition for allowance. If the Examiner should disagree, he is invited to contact the undersigned to discuss any remaining issues.

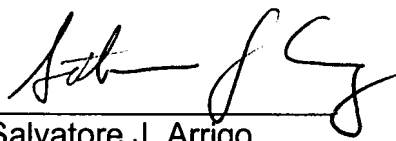
FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER L.L.P.

By: 

Salvatore J. Arrigo
Reg. No. 46,063
Tel: (202) 408-4000
Fax: (202) 408-4400
Email: arrigos@finnegan.com

Dated: October 4, 2002

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

MARKED-UP VERSION SHOWING CHANGES MADE TO SPECIFICATION

This is a continuation of application Serial No. 09/196,131, filed November 20, 1998, now U.S. Patent No. 6,238,924, which is a continuation of 08/417,226 filed, April 5, 1995, now U.S. Patent No. 5,962,327, which is a divisional of application Serial No. 07/971,160, filed November 5, 1992, now U.S. Patent No. 5,474,896, which is a continuation-in-part of application Serial No. 07/879,689, filed May 5, 1992, abandoned, all of which are incorporated herein by reference.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com